Combining Information: Heteroscedastic Random-Effects Models for Interlaboratory Comparisons

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Interlaboratory Studies:
The Scenario

- Each of p laboratories makes repeated measurements of m quantities (perhaps corresponding to different concentrations of a chemical analyte).

- The number of measurements made can differ among the laboratories.

- The measurement variability may depend on the material being measured (perhaps as an increasing function of concentration or level).

- The within-laboratory variabilities may differ (often, though, they are assumed to be equal).

Interlaboratory Studies: Some questions

- How should one estimate 'consensus' values of the quantities measured?

- What is the between-laboratory variability (*reproducibility*)?

- What is the within-laboratory variability (*repeatability*)? How do they compare?

- How should we look for outliers?

Why Interlaboratory Studies?

- Interlaboratory studies are primarily performed for one of two reasons:

  1. Validating a measurement method or standard material

  2. Assessing the proficiency of measurement laboratories.

Outline

- A single material measured by multiple laboratories − *one-way random model* (heteroscedastic and unbalanced)

    − Likelihood Analysis

    − Bayesian Model and Credible Regions

    − Example

- Some results for two-way models.

Dietary Fiber in Apricots
Li and Cardozo (1994)

Lab.	x_i	s_i^2	n_i
1	25.32	0.37	2
2	26.72	0.62	2
3	27.89	0.35	2
4	27.70	1.85	2
5	27.42	0.61	2
6	24.30	0.21	2
7	27.11	0.37	2
8	27.28	0.09	2
9	25.37	0.08	2

Mean: $\bar{x} = 26.567$

Weighted Means:

$$
\begin{aligned}
\text{MP} &= 26.472 \\
\text{GD} &= 26.164 \\
\text{ANOVA} &= 26.420 \\
\text{MLE} &= 27.275
\end{aligned}
$$

Statistical Framework:
One-Way, Unbalanced, Heteroscedastic Random-Effects ANOVA

- Laboratory sample means x_i distributed independently normal with mean μ and variance $\sigma^2 + \tau_i^2$, where $\tau_i^2 = \sigma_i^2/n_i$.

- Expected mean for ith laboratory is also normal, with mean μ and variance σ^2.

- Sufficient statistics x_i and $t_i^2 = s_i^2/n_i$.

If x_{ij} denotes the jth measurement from the ith lab, then

$$x_{ij} = \mu + b_i + e_{ij},$$

where $b_i \sim N(0, \sigma^2)$ and $e_{ij} = N(0, \sigma_i^2)$; mutually independent.

Maximum Likelihood
(Cochran, 1937)

Let $\omega_i = 1/(\sigma^2 + \tau_i^2)$, $\nu_i = n_i - 1$, and determine $\hat{\sigma}$, $\hat{\tau}_i^2$, and $\hat{\mu}$ to satisfy

$$(A_i) \quad \omega_i - \omega_i^2(x_i - \mu)^2 + \nu_i\left(\frac{1}{\tau_i^2} - \frac{t_i^2}{\tau_i^4}\right) = 0$$

$$(B) \quad \boxed{\sum_{i=1}^{k} \omega_i^2(x_i - \mu)^2 = \sum_{i=1}^{k} \omega_i}$$

$$(C) \quad \mu = \frac{\sum_{i=1}^{k} \omega_i x_i}{\sum_{i=1}^{k} \omega_i}$$

Note that (B) may have multiple roots. Cochran (1937) proposed setting $\tau_i^2 = t_i^2$ and solving (B) for σ^2, then using (C).

ML Equations

$$\mu = \frac{\sum_{i=1}^{p} \gamma_i x_i}{\sum_i \gamma_i} = \frac{\sum_{i=1}^{p} \omega_i x_i}{\sum_i \omega_i}$$

$$\sigma^2 = \frac{\sum_{i=1}^{p} \gamma_i \left[(x_i - \mu)^2 + \frac{\nu_i t_i^2}{1 - \gamma_i} \right]}{\sum_{i=1}^{p} n_i}$$

$$\gamma_i^3 - (a_i + 2)\gamma_i^2 +$$
$$[(n_i + 1)a_i + (n_i - 1)b_i + 1] \, \gamma_i$$
$$-n_i a_i = 0$$

where

$$\gamma_i \equiv \frac{\sigma^2}{\sigma^2 + \tau_i^2}$$

$$a_i \equiv \frac{\sigma^2}{(x_i - \mu)^2}$$

and

$$b_i \equiv \frac{t_i^2}{(x_i - \mu)^2}.$$

Result #1:
Monotone Convergence to Stationary Points of the Likelihood

- For any starting values μ_0, σ_0^2, maximize the likelihood over the weights by solving the cubics. (If there are multiple real roots, choose the one which causes the biggest increase in the likelihood.)

- Let

$$\sigma_1^2 = \frac{\sum_{i=1}^p \gamma_i \left[(x_i - \mu)^2 + \frac{\nu_i t_i^2}{1 - \gamma_i} \right]}{\sum_{i=1}^p n_i}$$

$$\mu_1 = \frac{\sum_{i=1}^p \gamma_i x_i}{\sum_{i=1}^p \gamma_i}$$

  solve for new weights, and iterate.

- This iteration, *regardless of starting values*, always converges to a stationary point of the likelihood, and *increases the likelihood at each step.*

Result #2:
Location of Stationary Values of the Likelihood

- At a stationary point of the likelihood,
$$\widehat{\sigma}^2 = \frac{\sum_{i=1}^{p} \gamma_i^2 (x_i - \mu)^2}{\sum_{i=1}^{p} \gamma_i}$$
  hence

- *All* of the stationary points of the likelihood $\widehat{\mu}$ and $\widehat{\sigma}$ are within the rectangle in the (μ, σ) plane given by
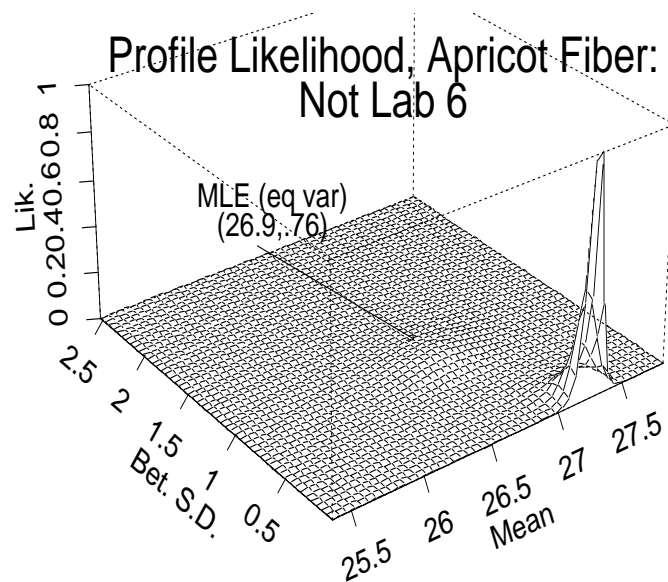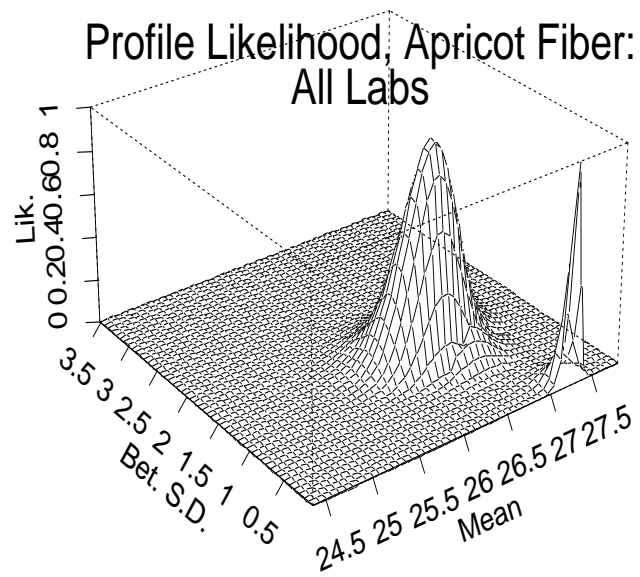$$\min_i(x_i) \leq \tilde{\mu} \leq \max_i(x_i)$$
  and
$$0 \leq \tilde{\sigma} \leq \max_i(x_i) - \min_i(x_i).$$

- After the appropriate location-scale transformation of the data, it is only necessary to search the unit square in the (μ, σ) plane for stationary values.

Lab. 6 an Outlier for Apricot Data

Profile Likelihood, Apricot Fiber: All Labs

Profile Likelihood, Apricot Fiber: Not Lab 6

MLE (eq var)
(26.9, .76)

Result #3:
Location of the Roots of Cubic Equations for Weights (γ_i)

- Each cubic likelihood equation has one or three roots $\gamma_i \in [0, 1]$.

- A necessary condition for three roots is that
$$(x_i - \mu)^2 \geq \max(\sigma^2/q_i, t_i^2/h_i),$$
where
$$
\begin{aligned}
q_i &= -2 - 6\sqrt{n_i} \sin\left\{ \frac{1}{3} \left[\sin^{-1}\left(\sqrt{\frac{n_i - 1}{n_i}} \right) - \frac{\pi}{2} \right] \right\} \\
&= \frac{8}{27 n_i} + O(n_i^{-2})
\end{aligned}
$$
and
$$
h_i = \frac{(1 - q_i)^3}{27(n_i - 1)} = \frac{1}{27 n_i} + O(n_i^{-2}).
$$

- These values q_i and h_i are the smallest for which this is necessary.

One-Way Models in Interlaboratory Studies: The Mandel-Paule Estimator J. of Research of the NBS (1982)

- For arbitrary positive weights $\{w_i\}_{i=1}^k$, weighted mean is

$$\tilde{\mu} = \frac{\sum_{i=1}^p w_i x_i}{\sum_{i=1}^p w_i}.$$

- *Mandel-Paule* estimate, μ_{MP}, of μ is the weighted mean $\tilde{\mu}$ for which

$$w_i \equiv \frac{1}{\tilde{\sigma}^2 + t_i^2}$$

where $\tilde{\sigma}^2$ is the root (if any) of

$$Q = \sum_{i=1}^p w_i (x_i - \tilde{\mu})^2 = p - 1$$

- Note: Q is convex decreasing on $[0, \infty)$, and $Q \sim \chi_{p-1}^2$ if

$$w_i = \omega_i \equiv \frac{1}{\sigma^2 + \tau_i^2}$$

The Mandel-Paule Algorithm and ML/REML

Maximum-Likelihood for a linear model

$$Y = X\beta + e,$$

where $e \sim \mathsf{N}\,(0, \Sigma)$ is equivalent to minimizing $|\Sigma|$, subject to

$$(y - X\widehat{\beta})^T \Sigma^{-1}(y - X\widehat{\beta}) = n \qquad (1)$$

where $\widehat{\beta}$ is the GLS estimate of β, and n is the number of observations.

For our one-way model, if the σ_i^2 are replaced by s_i^2, then (1), an equation in σ^2 alone, is

$$\sum_{i=1}^{p} w_i(x_i - \tilde{\mu})^2 = p.$$

Had REML been used, rather than ML, then the p on the RHS above would be a $p - 1$, *precisely* Mandel and Paule's equation.

Hierarchical Model With Noninformative Priors

$i = 1, \ldots, p$ indexes laboratories

$j = 1, \ldots, n_i$ indexes measurements

$$
\begin{aligned}
p(x_{ij}|\delta_i, \sigma_i^2) &= \mathsf{N}\,(\delta_i, \sigma_i^2) \\
p(\sigma_i) &\propto 1/\sigma_i \\
p(\delta_i|\mu, \sigma^2) &= \mathsf{N}\,(\mu, \sigma^2) \\
p(\mu) &= 1 \\
p(\sigma) &= 1
\end{aligned}
$$

A Useful Probability Density

Let T_ν and Z denote independent Student-t and standard normal random variables, and assume that $\psi \geq 0$ and $\nu > 0$. Then

$$U = T_\nu + Z\sqrt{\frac{\psi}{2}}$$

has density

$$f_\nu(u; \psi) \equiv \frac{1}{,_{\nu/2}\sqrt{\pi}} \int_0^\infty \frac{y^{(\nu+1)/2-1} e^{-y\left[1+\frac{u^2}{\psi y + \nu}\right]}}{\sqrt{\psi y + \nu}} dy.$$

Posterior of (μ, σ)

- Assume $\delta_i \sim \mathsf{N}(\mu, \sigma^2)$, $\sigma \sim p(\sigma)$,
  $p(\mu) = 1$, $p(\sigma_i) = 1/\sigma_i$.
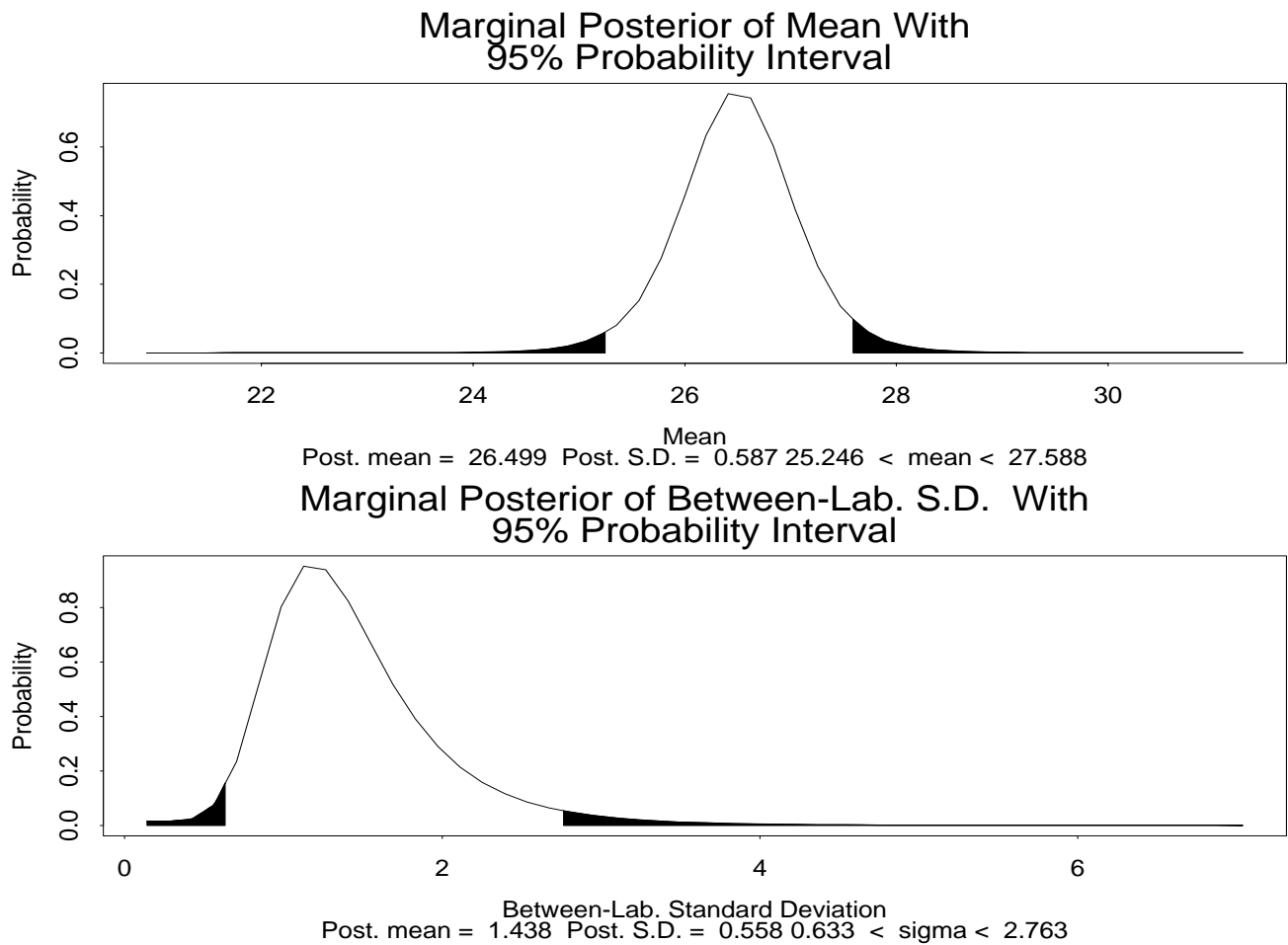
- Then the posterior of (μ, σ) is

$$p(\mu, \sigma | \{x_{ij}\}) \propto p(\sigma) \prod_{i=1}^{p} \frac{1}{t_i} f_{n_i-1} \left[\frac{x_i - \mu}{t_i}; \frac{2\sigma^2}{t_i^2} \right].$$

- The posterior of μ given $\sigma = 0$ is a product of scaled t-densities centered at the x_i, since

$$\frac{1}{t_i} f_{n_i-1} \left[\frac{x_i - \mu}{t_i}; 0 \right] = \frac{1}{t_i} T'_{n_i-1} \left(\frac{x_i - \mu}{t_i} \right).$$

- We will take $p(\sigma) = 1$, though an arbitrary proper prior does not introduce additional difficulties.

Approximate Confidence Intervals: Apricot Fiber Data

Marginal Posterior of Mean With 95% Probability Interval

Mean
Post. mean = 26.499 Post. S.D. = 0.587 25.246 < mean < 27.588

Marginal Posterior of Between-Lab. S.D. With 95% Probability Interval

Between-Lab. Standard Deviation
Post. mean = 1.438 Post. S.D. = 0.558 0.633 < sigma < 2.763

Small Simulation Comparing
Bayesian and Frequentist Intervals

$$\mu = 0$$
$$\sigma_i = \sigma_e$$
$$\sigma^2 + \sigma_e^2 = 1$$
$$\rho = \sigma^2/(\sigma_e^2 + \sigma^2) = 1/2$$

Simulation Comparing Confidence Intervals
(5 Groups of 5, rho=.5, mu=0, sigma =1)
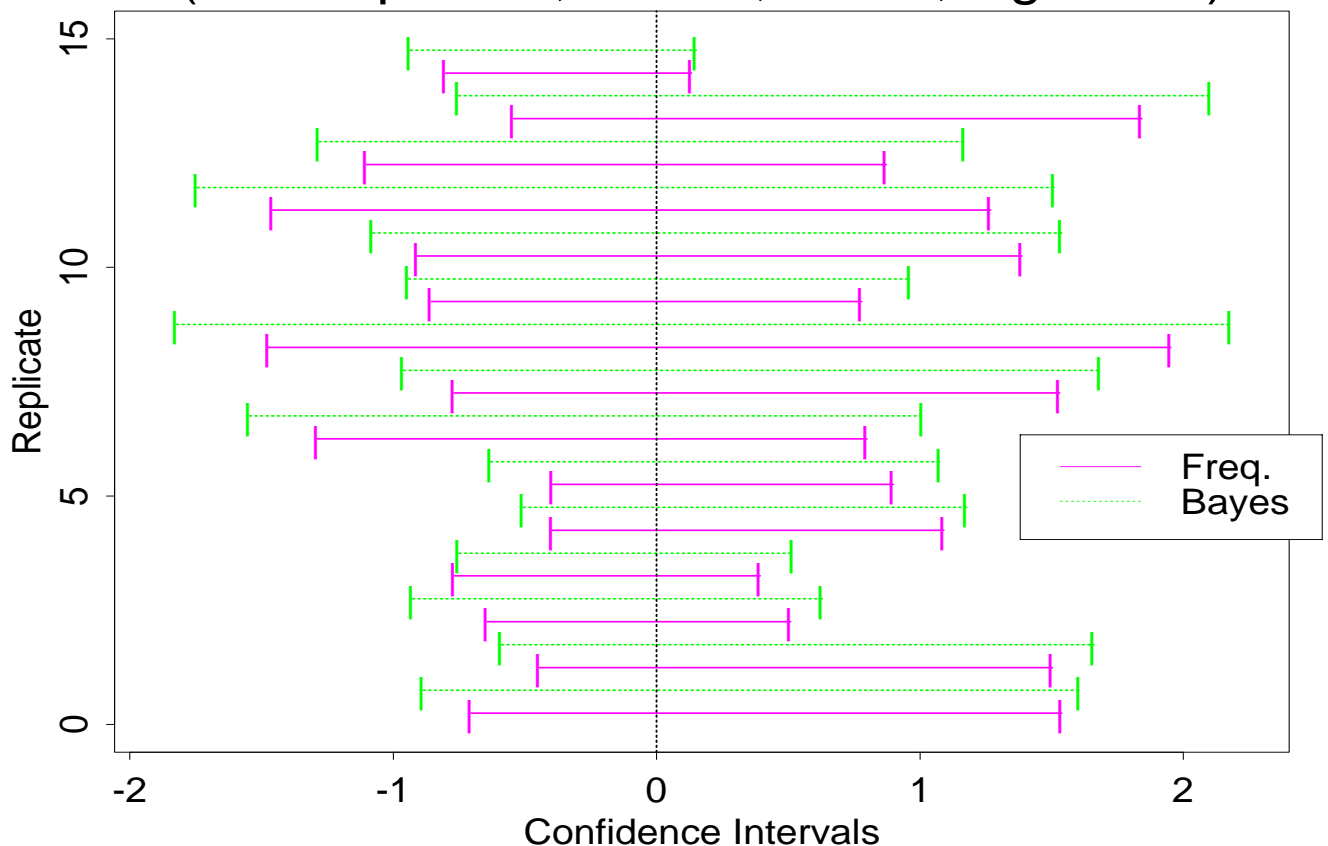
A Two-Way Mixed Model
(Heteroscedastic, no Interaction)

$$x_{ijk} = \theta_k + \delta_i + e_{ijk},$$

- $i = 1, \ldots, p$ Laboratories

- $j = 1, \ldots, n_i$ Replicates

- $k = 1, \ldots, m$ Materials

$$\delta_i \sim \mathsf{N}\left(0, \sigma^2\right)$$

$$e_{ijk} \sim \mathsf{N}\left(0, \sigma_i^2\right)$$

Some notation: $\tau_i^2 \equiv \sigma_i^2/(n_i m)$, $\nu_i \equiv n_i m - 1$.

ML Equations

$$\theta_k - \bar{\theta} \equiv \phi_k = \frac{\sum_{i=1}^{p}(\bar{x}_{i\cdot k} - \bar{x}_{i\cdot\cdot})/\tau_i^2}{\sum_{i=1}^{p} 1/\tau_i^2}$$

$$\bar{\theta} = \frac{\sum_{i=1}^{p} \gamma_i \bar{x}_{i\cdot\cdot}}{\sum_{i=1}^{p} \gamma_i}$$

$$\sigma^2 = \frac{\sum_{i=1}^{p} \gamma_i \left[(\bar{x}_{i\cdot\cdot} - \bar{\theta})^2 + \frac{\nu_i t_i^2}{1-\gamma_i}\right]}{\sum_{i=1}^{p} n_i}$$

Where $\tau_i^2 \equiv \sigma_i^2/(n_i m)$, $\nu_i \equiv mn_i - 1$, $\gamma_i \equiv \sigma^2/(\sigma^2 + \tau_i^2)$, and

$$t_i^2 \equiv \frac{\sum_{j,k}(x_{ijk} - \bar{x}_{i\cdot k})^2 + n_i \sum_k (\bar{x}_{i\cdot k} - \bar{x}_{i\cdot\cdot} - \phi_k)^2}{\nu_i n_i m}$$

ML Equations (Cont'd)

The weights $\{\gamma_i\}_{i=1}^p$ are roots of the cubic equations

$$
\begin{aligned}
&\gamma_i^3 - (a_i + 2)\gamma_i^2 + \\
&[(n_i m + 1)a_i + \nu_i b_i + 1]\,\gamma_i - \\
&n_i a_i = 0
\end{aligned}
$$

where

$$
a_i \equiv \frac{\sigma^2}{(\bar{x}_{i..} - \bar{\theta})^2}
$$

and

$$
b_i \equiv \frac{t_i^2}{(\bar{x}_{i..} - \bar{\theta})^2}.
$$

An ML Iteration

1. Begin with estimates $\left\{\gamma_i^{(s)}\right\}$.

2. Calculate the following:

$$\phi_k^{(s+1)} = \frac{\sum_{i=1}^{p}(\bar{x}_{i\cdot k}-\bar{x}_{i\cdot\cdot})/\tau_i^{2(s)}}{\sum_{i=1}^{p}1/\tau_i^{2(s)}}$$

$$\bar{\theta}^{(s+1)} = \frac{\sum_{i=1}^{p}\gamma_i^{(s)}\bar{x}_{i\cdot\cdot}}{\sum_{i=1}^{p}\gamma_i^{(s)}}$$

$$\sigma_{(s+1)}^2 = \frac{\sum_{i=1}^{p}\gamma_i^{(s)}\left[(\bar{x}_{i\cdot\cdot}-\bar{\theta})^2+\frac{\nu_i t_i^2}{1-\gamma_i^{(s)}}\right]}{\sum_{i=1}^{p}n_i}$$

3. Note that if the ϕ_k are constrained to satisfy the above ML equation, then

$$t_i^2 = \frac{\sum_{j,k}(x_{ijk}-\bar{x}_{i\cdot\cdot})^2 - \sum_k \phi_k^2/m}{n_i\nu_i m}$$

4. Solve the cubics for new estimates $\gamma_i^{(s+1)}$, and iterate.

Some Theoretical Results for Two-Way Mixed Model

The one-way results discussed earlier generalize:

- Monotone convergence

- All stationary values of likelihood in box in $(\mu, \sigma, \sum_k \phi_k^2)$ space.

- Exactly one weight $\gamma_i \in [0, 1]$, unless ith lab an outlier and n_i small

- Variances cannot be negative at solution to likelihood equation.

Summary

- A reparametrization of the likelihood in the one-way heteroscedastic model leads to new insights in likelihood and Bayesian analyses.

- A procedure of Mandel and Paule is equivalent to a modified REML estimator of the mean in an one-way heteroscedastic model.

- Many of these results carry over to two-way models; this work is ongoing.